Uraemic Toxin Concentration Variability in Haemodialysis Patients: Can we still rely on the results of cross-sectional studies?

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Background & Aim

Numerous cross-sectional studies evaluated in haemodialysis patients the **association** of specific uraemic toxin concentrations with patient **outcomes** at a given time point.

It has however never been investigated whether in stable patients, the pre-dialysis concentration of uraemic toxins remains constant.

We quantified the variability of uraemic toxin concentrations in haemodialysis patients over a period of 16 weeks.

Patients and Methods

Patients, Protocol & Sampling

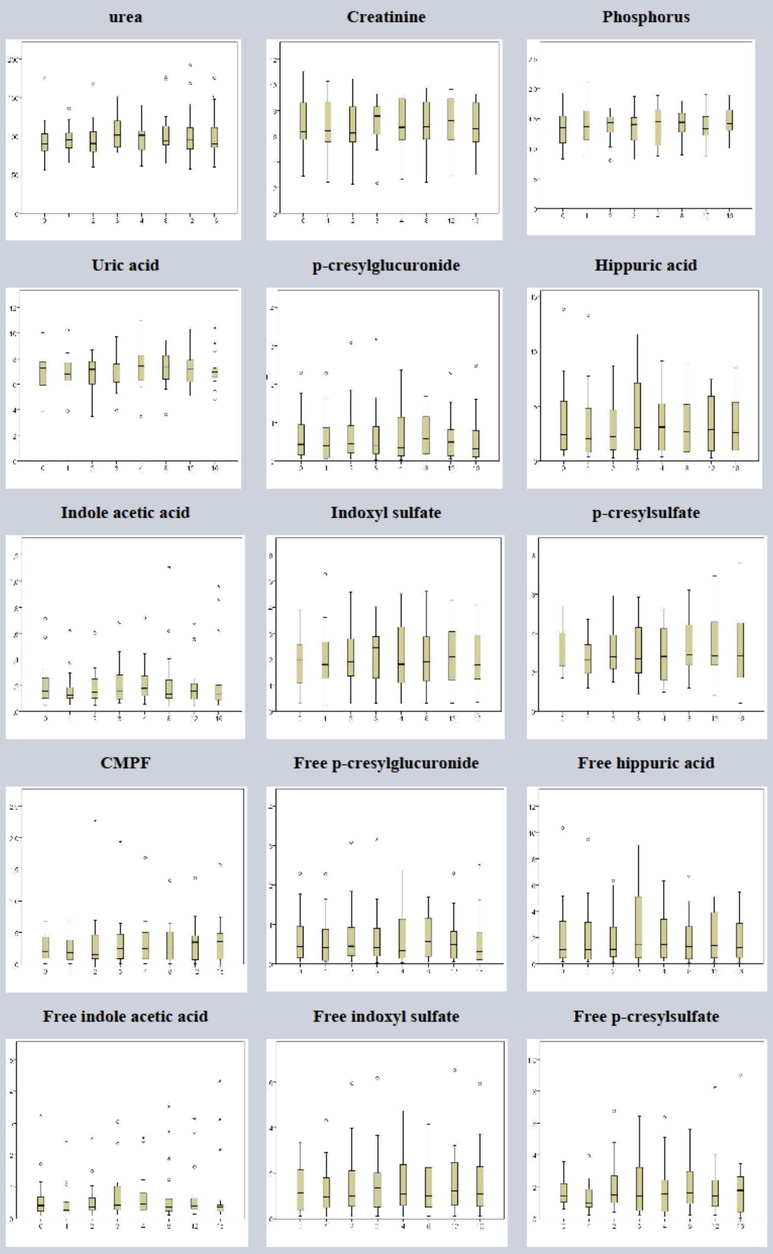
- We included **18 stable HD patients** (3 females, 11 diabetics, age 72.5±10.1y, vintage 55.7±30.1 months on HD, residual renal function 3.5±3.0mL/min 12 AVF, 5 double lumen CVC, and 1 graft combined with single lumen CVC)
- **Protocol** longitudinal **16 weeks midweek** follow-up
  maintaining dialyser (high flux) & HD mode (17 post HDF & 1 HD)
  blood and dialysate flow: 311±21 and 530±39mL/min
  ultrafiltration was set according to the need of the patient
- **blood sampling** **predialysis** of week 0, 1, 2, 3, 4, 8, 12, and 16
  blood was centrifuged + stored at -80°C

Laboratory & statistical analyses

- **Analytical determinations**
  - *small water soluble solutes*: urea, creatinine, phosphorus, uric acid
  - *protein-bound solutes PBS*: p-cresylglucuronide (PCG) hippuric acid (HA), indole acetic acid (IAA), indoxyl sulfate (IS), p-cresylsulfate (PCS), and 3-carboxy-4-methyl-5-propyl-2-furanpropionic acid (CMPF)
- **Statistics: intra- and inter-patient variability**:
  Variance Components analysis: Coefficient of variation %CV:
  [SDEV (=square of variance component)] / [mean of all data]
  Paired t-test to check differences between inter- and intra-patient %CV

Results

Inter-patient concentration variation (16 weeks)



Variance Components Analysis

		intra patient %CV	interpatient %CV
Urea		14.4	23.7
Creatinine		7.0	26.5
Phosphorus		13.6	15.7
Uric acid		10.1	16.6
p-cresylglucuronide	Total	38.7	95.1
	Free	40.4	96.2
Hippuric acid	Total	35.9	77.0
	Free	43.6	65.1
Indole acetic acid	Total	41.6	86.0
	Free	45.8	112.3
Indoxyl sulfate	Total	18.9	54.5
	Free	36.9	89.9
p-cresylsulfate	Total	22.6	41.8
	Free	38.0	84.5
CMPF	Total	25.4	118.1

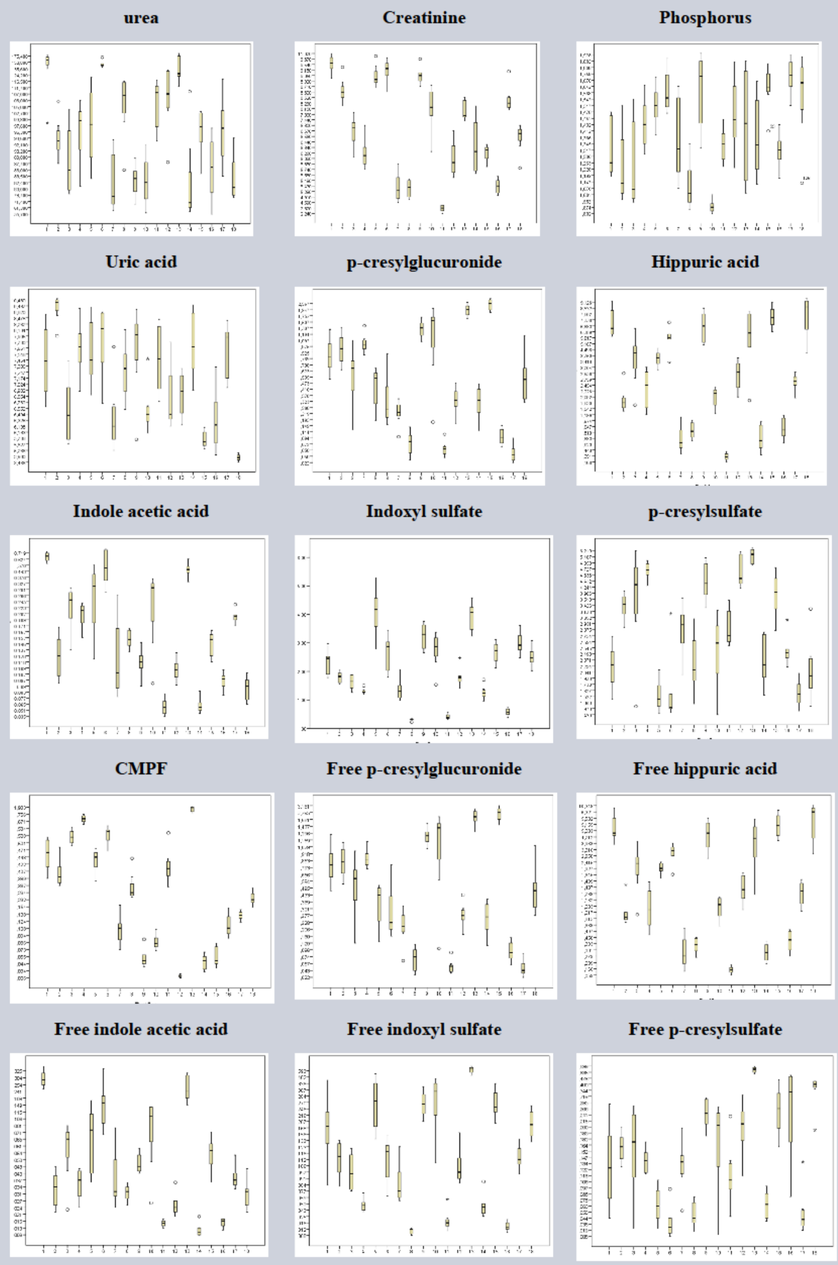
Kt/V was 1.6±0.3 with 13%CV (intra-patient) and 12%CV (inter-patient), and no trend in time.

The **intra-patient %CV** is in the range:
7-14% for small water soluble solutes
19%-25% for highly bound solutes IS, PCS, CMPF
36-46% for less bound solutes PCG, HA, and IAA, and for free concentrations of all studied PBS

The **inter-patient %CV** is in the range:
16-27% for small water soluble solutes
42-119% for total & free concentrations of PBS

Inter-patient %CV is significantly **larger** as compared to the intra-patient %CV ($p<0.001$).

Intra-patient concentration variation (18 patients)



Conclusion

Uraemic toxin concentrations vary largely among stable HD patients, but also intra-patient variability is non-negligible, especially for protein-bound solutes
It is unclear how intra-patient variability effects on the interpretation of association between toxin concentrations and outcomes.

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